REMARKS

The foregoing amendments and the following remarks are submitted in response to the communication dated June 29, 2004. The foregoing amendments to pages 12 and 93 of the Specification were made to correct an obvious error in the recitation of the percent (%) identity and the specific number of conservative and nonconservative amino acid differences among the N-terminal 100 amino acid residues of the mature mouse and human OB proteins. More specifically, at page 12, lines 11-12 the specification as filed states that

> "Overall, there is 84% identity at the amino acid level, ..."

and at page 93, lines 15-17, the specification as filed states that

> "Comparison of the human and mouse ob polypeptide sequences showed that the two molecules share an overall 84% identity at the amino acid level (Figure 4)."

However, Figure 4, which provides a comparison of the mouse and human amino acid sequences lined up to one another, demonstrates that there are 28 amino acid differences between the human and mouse sequences, out of a total of 167 amino acids. Thus, 139 amino acids, or 83% are identical. In addition, at page 93, lines 17-20, the specification states that

> "The N-termini of the mature proteins from both species share even higher homology, with only four conservative and three nonconservative amino acid substitutions among the N-terminal 100 amino acid residues."

However, Figure 4 demonstrates that there are in fact six conservative and six nonconservative amino acid substitutions among the N-terminal 100 amino acid residues of the mature mouse and human OB polypeptides. In view of cleavage of the OB polypeptide at the end of the signal sequence, after amino acid Alanine 21 (as detailed in the Specification, including at page 71, lines 14-21), the "N-terminal 100 amino acid residues" of the mature proteins corresponds to amino acids 22-122, starting with V (Valine). The skilled artisan can readily recognize that the mouse and human sequences from 22-122 show six conservative amino acid substitutions (specifically, R-K at 56, S-T at 71, V-I at 85, L-M at 89, L-I at 95 and L-V at 110) and six nonconservative amino acid substitutions (specifically, A-S at 53, Q-R at 92, A-S at 98, S-H at 118, Q-W at 121 and T-A at 122).

Applicants submit that this amendment does not introduce new matter into the specification because the correct percentage (%) of identity and the correct conserved and

nonconserved amino acid substitutions are readily determined from the amino acid sequences presented in Figure 4, or alternatively, by comparison of the amino acids depicted in the Specification in Figure 1 with 3 or those depicted in Figure 5 with 6. Further, Applicants submit that a person of ordinary skill in the art, upon review of Figure 4 and the sequences therein, would readily recognize the error and would realize that the correct number of conservative and nonconservative amino acid substitutions in the N-terminal 100 amino acid residues of the mature proteins and therefore that the percent identity is 83%.

Status of the Claims

Claims 59-83 are pending in the application. Claims 60 and 68 have been cancelled without prejudice. Claims 59, 61-67, 69-74 and 79 have been amended in order to more particularly point out and distinctly claim that which Applicants regard as the invention. New claims 84-88 are presented. Support for the amended claims can be found generally through Applicants' specification.

Claim Objections

Claims 71-83 are objected to under 37 CFR 1.75(c) as being in improper format in as much as a multiply dependent claim cannot depend from another multiply dependent claim. Applicants have above cancelled claim 68 and amended claims 71 to 74 and 79 and now present new claims 84 to 88 so as to correct the claim dependencies and present them in proper form without multiple dependencies. In view of the above amendments, Applicants respectfully request that the Examiner accept claims 71 to 88 and treat these claims on the merits.

The Specification Fully Describes the Claimed Invention

The Examiner has rejected claims 59-60, 63 and 68-70 under 35 U.S.C. 112, first paragraph, as failing to comply with the written-description requirement, asserting that the claims contain subject matter which was not described in the specification so as to convey that

the inventors had possession of the claimed invention at the time of filing.

Claim 59, part (d), directed to "a nucleic acid sequence that hybridizes to any one of the nucleic acids of (a), (b), and (c)", is rejected because the Examiner asserts that the recitation encompasses any hybridization condition and therefore any nucleic acids in existence. Applicants have above amended claim 59 to provide hybridization conditions, as supported by the Specification.

Claim 60 is rejected as being directed to species of protein which are not described in the specification as to convey to one skilled in the act that the inventor (s) had possession of the claimed invention at the time of filing. Applicants respectfully disagree. Claim 60 refers to a mammalian OB polypeptide having the sequence of a naturally occurring mammalian OB polypeptide and having a mature protein about 145 amino acids. Support for mammalian OB polypeptide is found particulary in the cloning and characterization of OB encoding polynucleotides from both mouse and human mammalian species, as provided in the Specification and in SEQ ID NO:1 and SEQ ID NO:3 respectively. In addition, Figure 16 of the specification (as discussed on page 16, lines 3-10 and on page 93, lines 21-28) demonstrates cross-hybridizing genomic DNA in mouse, rat, rabbit, vole, cat, cow, sheep, pig, chicken, eel, and drosophila using labeled mouse OB exon 2G7 as a probe, indicating that OB encoding polypeptides are readily obtainable using the specifically disclosed polynucleotides. Methods for obtaining the OB gene encoding DNA from these and other species are described in the specification at pages 38-40 and were well known in the art even as of the priority date of this application. Methods for determining an encoded OB polypeptide's ability to modulate body weight as is called for by Claim 60 are also described in the Specification, including the assessment of the ability of the OB polypeptide to decrease body fat when purified OB polypeptide is administered, and may be carried out by a person of ordinary skill in the art using routine methods and without undue experimentation. Such activity is determined simply by administering to an animal the polypeptide and measuring the weight change in that animal. Other tests are also described in the Specification. For example, pages 55-58 of the Specification describes how the ordinarily skilled artisan may characterize the biological activity of OB analogs through initial *in vitro* tests, e.g. specific binding to an OB antibody. In an effort to facilitate Examination and without prejudice to further prosecution, however, Applicants have

above cancelled claim 60, making this rejection moot.

Claim 63 is rejected for new matter for the recitation of "83 percent or greater amino acid sequence identity". Applicants respectfully submit that the specification provides support for the 83% recitation, including in the comparison of the disclosed amino acid sequences of mouse and human OB polypeptides. Specifically the Specification characterizes the percentage (%) identity between the mouse and human OB amino acid sequences, where at page 11, line 25, the specification *now* states that

"Overall, there is 83% identity at the amino acid level, ..."

and at page 72, lines 8-10, the specification now states that

"Comparison of the human and mouse ob polypeptide sequences showed that the two molecules share an overall 83% identity at the amino acid level (Figure 4)."

In addition, Figure 4, which provides a comparison of the mouse and human amino acid sequences aligned with one another, demonstrates that there are 28 amino acid differences between the human and mouse sequences, out of a total of 167 amino acids. Thus, 139 amino acids, or 83%, are identical, i.e. Alanine for Alanine, Glutamine for Glutamine. It is believed to be particularly straightforward for the skilled artisan to make such a comparison since the length of the mouse and human OB polypeptides are the same and the corresponding amino acids to compare in assessing identity is very readily determined -no gaps exist and no accounting for regions of extra amino acids is necessary. In addition, the skilled artisan's comparison of SEQ ID NO: 5 (which is the mouse variant OB polypeptide with glutamine 49 deleted) with SEQ ID NO:6 (which is the human variant OB polypeptide with glutamine 49 deleted) will yield the same result of 83% amino acid identity in a similarly straightforward fashion.

The Specification Fully Enables the Claimed Invention

Claim 59 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. This rejection is directed at subpart e) of claim 59, the language of which has been deleted by amendment above. Applicants submit that this rejection is now made moot.

In view of the foregoing remarks, Applicants submit that the Examiner's rejections under 35 U.S.C. 112, first paragraph, may properly be withdrawn

Particularity and Distinctiveness of the Claims

The Examiner has rejected claims 59-70 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter applicant regards as the invention.

The Examiner rejects Claim 59 parts d) and e) in the recitation of "a nucleic acid sequence" which lacks antecedent basis. Applicants have above amended claim 59 subparts d) and e) to recite "a nucleic acid molecule", which has proper antecedent basis.

Claims 60-67 have been rejected in the recitation of "having one or more polymers attached thereto" and "optionally in a pharmaceutical carrier". The Examiner asserts that it is not clear if these recitations are directed at the nucleic acid molecules or at the polypeptide. Applicants have above amended claims 60-67 to address this rejection and clarify the claim recitation language.

Claims 64-67 are rejected as unclear and lacking antecedent basis for the OB polypeptide variant and having no structure recited for the OB polypeptide. Claims 64-67 have been above amended to address this rejection and to properly reference a particular structure or sequence for the OB polypeptide variant.

In view of the foregoing amendments and remarks, Applicants submit that the Examiner's above noted rejections under 35 U.S.C. 112, second paragraph, may be properly withdrawn.

The Double Patenting Rejection

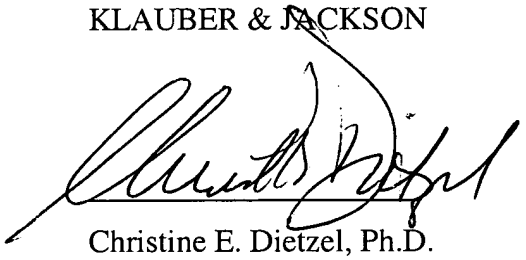
The Examiner has provisionally rejected claims 59-70 under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 5,935,801 and claims 1-21 of U.S. Patent No. 6,309,853. In as much as this rejection is provisional, Applicants acknowledge this rejection and recognize it as provisional at present. The issue will be readdressed by Applicants at such time as other patentability issues are settled.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,

KLAUBER & JACKSON



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